

Protocol Title: Evaluation of 5-Hour ENERGY® drink
on the blood pressure and electrocardiographic
parameters on young healthy volunteers: A randomized,
double blind, crossover, placebo-controlled trial
FDG20110007H

Shah

DGMC Human Research Final Report Template

60th Medical Group (AMC), Travis AFB CA
INSTITUTIONAL REVIEW BOARD (IRB)
Non-Exempt Study Final Report

(Please type all information. Use additional pages if necessary.)

Protocol #:FDG20110007H

Initial Approval Date: 22 Feb 2011

Date report Submitted: 29 Jan 2014

Protocol Title: Evaluation of 5-Hour ENERGY® drink on the blood pressure and electrocardiographic parameters on young healthy volunteers: A randomized, double blind, crossover, placebo-controlled trial.

Principal Investigator: Sachin Shah, Pharm D

Office Symbol: SGQP

Phone: 707-423-3277

APPROVED

60MDG IRB
TRAVIS AFB CA

1. Protocol Type

Greater than Minimal Risk Minimal Risk

2. Protocol Outcome Summary

Were the protocol objectives met, and how will the outcome benefit the DOD/USAF?

1) Please see poster for detailed results

2) The data is relevant to the DOD and shows:

- a. When consumed appropriately, 5 Hour Energy does not prolong the QT interval
- b. Blood pressure is increased but is not elevated enough to cause an acute threat
- c. DOD personnel should not consume energy drinks outside the recommended doses
- d. DOD personnel with hypertension or those of older age should exercise caution when consuming energy drinks
- e. Current evidence does not warrant a cardiac threat enough to warrant placing restrictions on the appropriate use of energy drinks by DOD personnel

3. Protocol Status

(Check one only)

- Inactive, protocol never initiated
 Inactive, protocol initiated but has not/will not be completed
 All approved procedures/uses have been completed

Report Documentation Page		Form Approved OMB No. 0704-0188
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1. REPORT DATE 11 FEB 2014	2. REPORT TYPE Final	3. DATES COVERED 22 Feb 2011 - 11 Feb 2014
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		5b. GRANT NUMBER
		5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) Dr. Sachin Shah, Lt Col Michael Lee, Lt Col Nicholas Milazzo, Capt Anthony Dargush, Maj Carolyn Lacey		5d. PROJECT NUMBER FDG20110007H
		5e. TASK NUMBER
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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Clinical Investigation Facility David Grant Medical Center 101 Bodin Circle Travis AFB, CA 94535		8. PERFORMING ORGANIZATION REPORT NUMBER
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13. SUPPLEMENTARY NOTES		
14. ABSTRACT <p>INTRODUCTION: The impact of energy drinks on the cardiac rhythm remains unknown. QT/QTc interval prolongation has been known to induce life threatening arrhythmias. We sought to determine the impact of 5-Hour Energy shot on the QTc interval after acute and chronic consumption. METHODS: This was a randomized, placebo controlled, crossover study enrolling young healthy volunteers not on any medications. Subjects received the study drink (5 Hour Energy shot or placebo) twice daily separated by approximately 7 hours for the first 7 days. This was followed by a washout period of 6 days and the alternate study drink was consumed for the final 7 days. A 12-lead electrocardiogram (ECG) was performed at baseline, 1, 3 and 5 hours on days 1, 7, 15 and 21. The automated ECG measurements were used for per-treatment and ITT analysis and analyzed using the paired t-test. RESULTS: A total of 24 subjects (29 ± 5.8 years) were included for analysis. QTc values after consumption of a single placebo-dose were 414 ± 18, 413 ± 15, 413 ± 19 and 417 ± 19 milliseconds at baseline, 1, 3 and 5 hours respectively. Post consumption of a single 5 hour Energy dose, QTc values were 415 ± 17, 408 ± 19, 410 ± 20, and 413 ± 17 milliseconds at baseline, 1, 3 and 5 hours, respectively (all time matched inter- group p-values > 0.292). QTc values after consumption of placebo for 7 days were 415 ± 20, 413 ± 18, 409 ± 19, and 413 ± 22 milliseconds at baseline, 1, 3 and 5 hours, respectively. Post consumption of 5 hour Energy for 7 days, resulted in QTc values of 415 ± 22, 413 ± 24, 415 ± 24, and 415 ± 21 milliseconds at baseline, 1, 3 and 5 hours, respectively (all time matched inter- group p-values > 0.198). There was no difference between the PR interval, QRS duration, QT interval and heart rate between the two groups. CONCLUSION: 5-Hour Energy did not induce any significant changes in the QTc interval or other ECG parameters after single and multiple doses throughout a 7 day period. These results may vary between different energy drinks due to the varying ingredients within them.</p>		

15. SUBJECT TERMS

US Air Force, Medical Service, Medical Research, Graduate Medical Education

16. SECURITY CLASSIFICATION OF:

a. REPORT

unclassified

b. ABSTRACT

unclassified

c. THIS PAGE

unclassified17. LIMITATION OF
ABSTRACT**UU**18. NUMBER
OF PAGES**2**19a. NAME OF
RESPONSIBLE PERSON**Standard Form 298 (Rev. 8-98)**

Prescribed by ANSI Std Z39-18

4. Number of Subjects Enrolled and Status of Subjects

Twenty-seven subjects were enrolled and began participation in the study. Twenty-five completed the study. Two subjects withdrew, 1 could not commit to the time and the other subject experienced adverse event of nausea and headache.

Seven other subjects signed consent forms but never actually began the study. Three had time constraints at work that prevented them from participating and 4 had pre-existing conditions that prevented them from progressing further in the study.

5. Number of Amendment(s) to Protocol: 9

Date(s) of Amendments: Amendment 1, 24 May 11; Amendment 2, 19 Aug 11;
Amendment 3, 01 Nov 11; Amendment 4, 12 Jul 12; Amendment 5, 21 Sept 12; Amendment 6,
17 Oct 2012; Amendment 7, 25 October 12; Amendment 8, 28 Feb 2013; Amendment 9, 06
May 2013

6. Funding

Source of Funding: Surgeon General Office

Funding allocated since start of study \$5430.00 Funds remaining \$0.00

7. Protocol Personnel Changes

Have there been any Principal or Associate Investigator Personnel changes since approval, last review protocol, or annual review?

Yes No

Name	Rank	Study Role	Date of Investigator Training	Staff/ Resident/ Fellow/ Civilian	Dept/ Office Symbol	Addition or Deletion	Date of Change
Michael Lee	Lt Col	PI	10/16/10	Staff	SGQP	Changed from PI to AI	12 Jul 12
Sachin Shah	CTR	AI	10/31/13	STAFF	SGQP	Changed from AI to PI	12 Jul 12
Nicholas Milazzo	Lt Col	AI	10/12/11	Staff	SGSE	Add as AI	12 Jul 12
Michael Lee	Lt Col	AI	10/16/10	Staff	SGBH (WHASC)	Deleted as AI	6 May 13

8. Adverse Events and Unanticipated Events

Identify any problems or adverse events that have affected study progress.

a. Had unexpected events been reported to the IRB? Yes No N/A

If yes, please describe _____

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FDG#: 201100074

SachinShah
(Insert PI's last name here)
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9. **Manpower**

List manpower expended on this study

Rank	AFSC	# hours duty time	# hours off-duty time
LtCol Michael Lee	43P	5	0
Capt Anthony Dargush	43PX	40	0
LtCol Nicholas Milazzo	43PX	5	0
Maj Carolyn Lacey	44M3B	20	0
Vicki Potts	Contractor	750	0
Sachin A Shah	Contractor	200	0

10. If this was an EMERGENCY protocol, attach a copy of the narrative summary.

N/A

11. **Publications**

Were there any publications as a result of this research?

American Heart Association, Scientific Sessions, November, 2013. POSTER (attached)

Sachin A Shah

1/29/14

(PI / AI Signature)

(Date)

ADVERSE EVENTS FOR THE 5 HOUR ENERGY DRINK STUDY.

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As reported to the IRB at the last continuing review January 2013, the adverse events that subjects reported during the course of the study are as follows:

7 patients experienced palpitations or increased heart rate.

6 patients reported being shaky/jittery or nervous

6 patients reported upset or nausea

4 patients reported headache

5 patients reported sleeplessness

3 patients reported being lightheaded or dizzy

3 reported facial flushing

1 reported vomiting

1 reported diarrhea

1 report of being "hyper"

1 report of appetite suppression

1 report of being edgy (not Jittery)

All adverse events were resolved by the time each patient had completed their portion of the study no residual effects. None of these were deemed serious or unexpected.

A handwritten signature in black ink, appearing to read "S. J.", is positioned below the statement about adverse events.



Impact of Acute and Chronic 5-Hour Energy Consumption on Electrocardiographic and Blood Pressure Parameters

Sachin A Shah, PharmD;^{a,b} Carolyn S Lacey, MD;^b Vicki Potts, RN;^b Christopher M Lopez;^b Ian C Riddock,^b MD; Michael Lee, PharmD;^b Nicholas Milazzo, PharmD;^b Anthony E Dargush, PharmD;^b
a) University of the Pacific, Thomas J Long School of Pharmacy and Health Sciences, Stockton, CA; b) David Grant USAF Medical Center, Travis Air Force Base, CA



ABSTRACT

INTRODUCTION: The impact of energy drinks on the cardiac rhythm remains unknown. QT/QTC interval prolongation has been known to induce life threatening arrhythmias. We sought to determine the impact of 5-Hour Energy shot on the QTc interval after acute and chronic consumption.

METHODS: This was a randomized, placebo controlled, crossover study enrolling young healthy volunteers not on any medications. Subjects received the study drink (5 Hour Energy shot or placebo) twice daily separated by approximately 7 hours for the first 7 days. This was followed by a washout period of 6 days and the alternate study drink was consumed for the final 7 days. A 12-lead electrocardiogram (ECG) was performed at baseline, 1, 3 and 5 hours on days 1, 7, 15 and 21. The automated ECG measurements were used for pre-treatment and ITT analysis and analyzed using the paired t-test.

RESULTS: A total of 24 subjects (29±5.8 years) were included for analysis. QTc values after consumption of a single placebo dose were 414±18, 413±15, 413±19 and 417±19 milliseconds at baseline, 1, 3 and 5 hours respectively. Post consumption of a single 5 hour energy dose, QTc values were 415±17, 408±19, 410±20, and 413±17 milliseconds at baseline, 1, 3 and 5 hours, respectively (all time matched inter-group p-value > 0.292). QTc values after consumption of placebo for 7 days were 415±20, 413±18, 409±19, and 413±22 milliseconds at baseline, 1, 3 and 5 hours respectively. Post consumption of 5 hour Energy for 7 days, resulted in QTc values of 415±22, 413±24, 415±24, and 415±21 milliseconds at baseline, 1, 3 and 5 hours, respectively (all time matched inter-group p-values >0.198). There was no difference between the PR interval, QRS duration, QT interval and heart rate between the two groups.

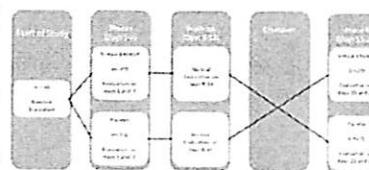
CONCLUSION: 5 Hour Energy did not induce any significant changes in the QTc interval or other ECG parameters after single and multiple doses throughout a 7 day period. These results may vary between different energy drinks due to the varying ingredients within them.

INTRODUCTION

- From 2008 to 2012, the market for energy drinks increased by 60%, resulting in sales of more than \$12.5 billion.
- The number of emergency department visits involving energy drinks has been steadily rising from 10,668 in 2007 to 20,738 in 2011. Of those visits, 55% involved only energy drinks while the remaining 42% involved energy drinks in combination with other substances.
- There have been reports of atrial fibrillation, Takotsubo cardiomyopathy and sudden cardiac death in healthy individuals after energy drink consumption.
- The FDA does not regulate nutraceuticals as rigorously as new drug entities and the safety of energy drink consumption needs further exploration.
- The goal of this study is to assess the acute and chronic effects of 5-Hour Energy consumption on electrocardiographic and hemodynamic parameters in healthy human subjects.

METHODS

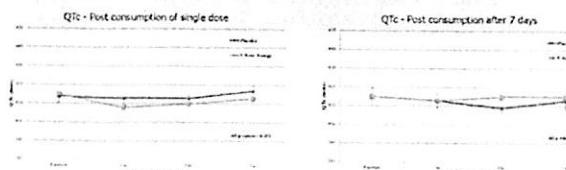
- This was a randomized, double blind, placebo controlled, crossover study.
- This study planned to enroll 40 subjects.
 - Inclusion Criteria: healthy individuals between 18 and 40 years of age.
 - Exclusion Criteria: abnormal baseline cardiac rhythm, history of atrial or ventricular arrhythmia, baseline corrected QT (QTc) interval greater than 440 milliseconds (msec), concurrent use of drugs potentially interacting with either 5-Hour Energy drink or effecting electrocardiographic or hemodynamic parameters, or having consumed any type of energy drink within one week prior to randomization.
- Endpoints: QTc interval, office systolic blood pressure (SBP), office diastolic blood pressure (DBP), ambulatory SBP and DBP, PR interval, QRS complex duration and heart rate.
- Intervention: 2 shots separated by 7 hours of either 5-Hour Energy or matching placebo daily for 7 days.
- 12-lead ECG and office blood pressure were measured at baseline and at 1, 3 and 5 hours post consumption on days 1, 7, 15 and 21.
- Intergroup comparisons were performed using a paired student's t-test.



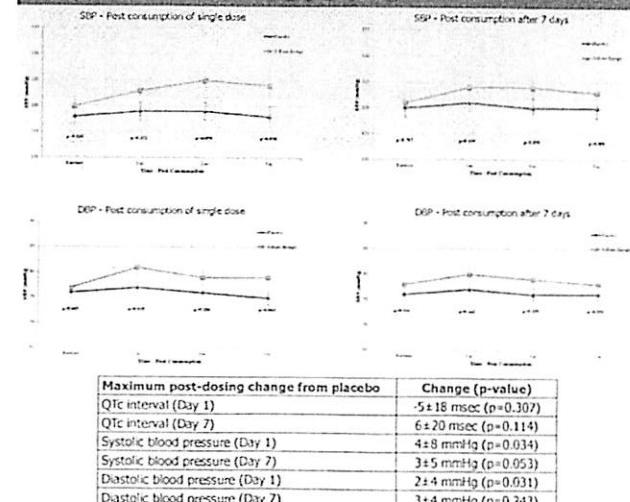
RESULTS

Twenty four subjects were included for analysis:

- Age: 26.4 ± 5.8 years
- Weight: 167.2 ± 30.1 kg
- Height: 68.4 ± 3.6 inches
- Male: 77.8%
- Caucasian: 77.8%



RESULTS



Differences in PR interval, QRS duration and heart rate between the two groups were non-significant.

CONCLUSIONS

- 5-Hour Energy did not significantly prolong the QTc interval or any other ECG parameters after a single shot or post 7 days of consumption.
- A single dose of 5-Hour Energy significantly increased SBP and DBP but the effects appear to diminish with chronic consumption.
- Future studies are needed to further assess the cardiac effects of energy drinks using differing products, doses, populations and duration of consumption.

The views expressed in this material are those of the authors, and do not reflect the official policy or position of the U.S. Government, the Department of Defense or the Department of the Air Force.